

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 572	FOR FURTHER ACTION		See item 4 below
International application No. PCT/IL2004/000732	International filing date (<i>day/month/year</i>) 05 August 2004 (05.08.2004)	Priority date (<i>day/month/year</i>) 07 August 2003 (07.08.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant APPLIED RESEARCH SYSTEMS ARS HOLDING N.V.			

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1 (a).																
2.	This REPORT consists of a total of 6 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 15%;"><input checked="" type="checkbox"/> Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/> Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/> Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/> Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/> Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/> Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/> Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/> Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/> Box No. I	Basis of the report	<input type="checkbox"/> Box No. II	Priority	<input type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/> Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/> Box No. VI	Certain documents cited	<input type="checkbox"/> Box No. VII	Certain defects in the international application	<input type="checkbox"/> Box No. VIII	Certain observations on the international application
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4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 740 14 35</p>	<p>Date of issuance of this report 13 February 2006 (13.02.2006)</p> <hr/> <p>Authorized officer</p> <p style="text-align: center; font-size: 1.2em;">Simin Baharlou</p> <p>Telephone No. +41 22 338 71 30</p>
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PATENT COOPERATION TREATY

REC'D 05 JAN 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

17/2

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IL2004/000732

International filing date (day/month/year)
05.08.2004

Priority date (day/month/year)
07.08.2003

International Patent Classification (IPC) or both national classification and IPC
C07K1/20, C07K1/22, C07K14/47, C07K14/715, C07K14/54, C07K19/00, A61K38/04

Applicant
APPLIED RESEARCH SYSTEMS ARS HOLDING N.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IL2004/000732

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IL2004/000732

**Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-40
	No: Claims	41-45
Inventive step (IS)	Yes: Claims	
	No: Claims	1-45
Industrial applicability (IA)	Yes: Claims	1-45
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO-A-03059376 (Yeda Research & S Haggiag), 24 July 2003;
- D2: EP-A-0 006 035 (Natl. Res. Dev. Corp.), 12 December 1979;
- D3: WO-A-0104276 (Université de Liège), 18 January 2001;
- D4: Blood 94 (3), 1 August 1999, pages 923-931;
- D5: Eur. Cytokine Network 8 (4), December 1997 (1997-12), pages 359-365;
- D6: Cytokine 14 (6), 21 June 2001, pages 334-342;
- D7: J. Immunol. 168 (7), 1 April 2002, pages 3608-3616;
- D8: J. Chromatogr. A 952 (1-2), 2002, pages 99-110;
- D9: Trends in Biotechnology 20 (8), August 2002, pages 333-337;
- D10: J. Chromatogr. A 908, 2001, pages 251-263;
- D11: J. Chromatogr. A 814, 1998, pages 71-81.

1) D1 discloses the use of pure IL6-IL6r chimera in nerve cell regeneration. In the text allusion is made to the fact that this hybrid protein has been purified using affinity chromatography (Example 2). The process in question is alluded also in D4 and disclosed in D5 (see section Materials and Methods). D2 and D3 disclose the purification of two different beta-galactosidases from different sources. D6 and D7 disclose the use of affinity chromatography to purify IL18BP. Therefore claims 41-45, referring to a protein of this sort purified with the use of hydrophobic charge induction chromatography (HCIC), are considered not to be new under Art. 33(2) PCT. It should be considered that a new purification method does not automatically confer novelty to a known product obtained through the method in question (product-by-process claim).

2) D8-D11 disclose the purification of several proteins by HCIC, including antibodies and non-antibody proteins. The difference between the above documents and the present application consists in the fact that HCIC is used for the preparation of non-immunoglobulin proteins containing immunoglobulin-like domains. The applicant has provided functional tests demonstrating that HCIC can indeed be used for the above purification. However, when the skilled artisan considers this form of process, two things become immediately evident. The first is that HCIC is an election method for the preparation of antibodies, thus by definition proteins containing immunoglobulin

domains. The second is the fact that the use of HCIC can be generalized to several other proteins and enzymes (see especially D8 and D10). The first evidence would induce the skilled person to try and use HCIC for the purification of proteins having immunoglobulin-like domains. The identification of such proteins is no longer a problem since the different sequence data bases offer the practitioner complete knowledge of a given sequence and can compare it with any other sequence. Thus the identification of proteins containing immunoglobulin-like domains would require no undue effort from the skilled artisan. The skilled artisan, moreover, would be immediately be induced to try HCIC on proteins different from antibody by the versatility of the method, which can be used on different classes of proteins beyond antibodies (D8 and D10). On the basis of these considerations it is considered that claims 1-40 are not inventive under Art. 33(3) PCT.